PATHOLOGY TEAM

Pathology and mechanisms of malabsorption

Done by:

Bader Al ghamdi & Wala' Al shehry

Pathology and mechanisms of malabsorption

DIARREAHA

Definition: 3 or more loose or liquid stools per day
Abnormally high fluid content of stool
> 200-300 gm/day

Classification

1. *Acute ……..if* 2 weeks,
2. *Persistent ……. if 2 to 4 weeks,*
3. *Chronic ……..if 4 weeks in* duration.

WHY Diarreaha IMPORTANT?

The loss of fluids through diarrhea can cause dehydration and electrolyte imbalances. Easy to treat but if untreated, may lead to death especially in children

Fecal Osmolarity

As stool leaves the colon, fecal osmolality is equal to the serum osmolality i.e. 290mosm/kg. Under normal circumstances, the major osmoles are Na^+, K^+, Cl^-, and HCO_3^-.

Pathophysiology and Categories of diarrhea

1. Secretory
2. Osmotic
3. Exudative (inflammatory)
4. Motility-related

Secretory

-There is an increase in the active secretion

-High stool output

-Lack of response to fasting

-Normal stool osmotic gap < 100 mOsm/kg

-The most common cause of this type of diarrhea is a bacterial toxin (E. coli , cholera) that stimulates the secretion of anions.

Also seen in Endocrine tumours

Osmotic

-Excess amount of poorly absorbed substances that exert osmotic effect……water is drawn into the bowels……diarrhea

-Stool output is usually not massive

-Fasting improve the condition

-Stool osmotic gap is high, > 125 mOsm/kg

Can be the result of

1. Malabsorption in which the nutrients are left in the lumen to pull in water e.g. lactose intolerance
2. osmotic laxatives.

Exudative (inflammatory)

Results from the outpouring of blood protein, or mucus from an inflamed or ulcerated mucosa. Presence of blood and pus in the stool.

- Persists on fasting
- Occurs with inflammatory bowel diseases, and invasive infections.

Motility Related

Caused by the rapid movement of food through the intestines (hypermotility).

Irritable bowel syndrome (IBS) – a motor disorder that causes abdominal pain and altered bowel habits with diarrhea predominating

Approximately 80% of acute diarrheas are due to *infections* (viruses, bacteria, helminths, and protozoa)./ Viral gastroenteritis (viral infection of the stomach and the small intestine) is the most common cause of acute diarrhea worldwide. / Food poisoning / Drugs / Others

Antibiotic-Associated Diarrheas

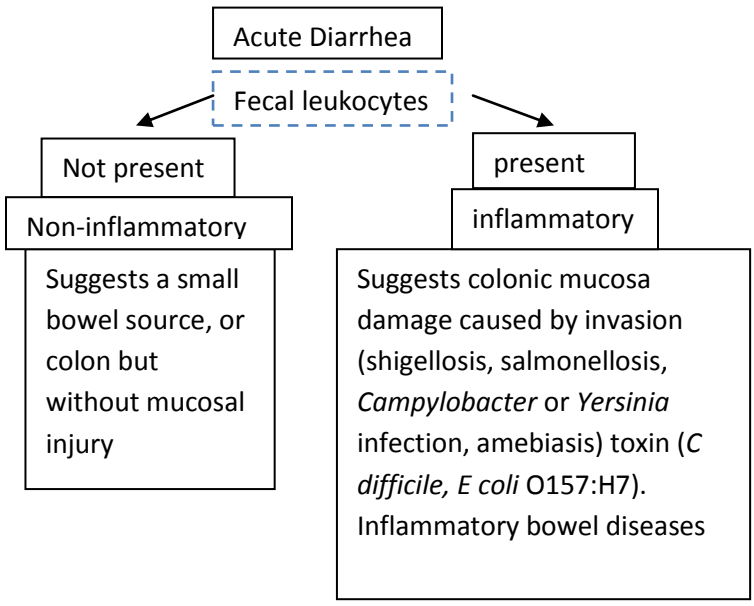
Diarrhea occurs in 20% of patients receiving broad-spectrum antibiotics; about 20% of these diarrheas are due to *Clostridium difficile*

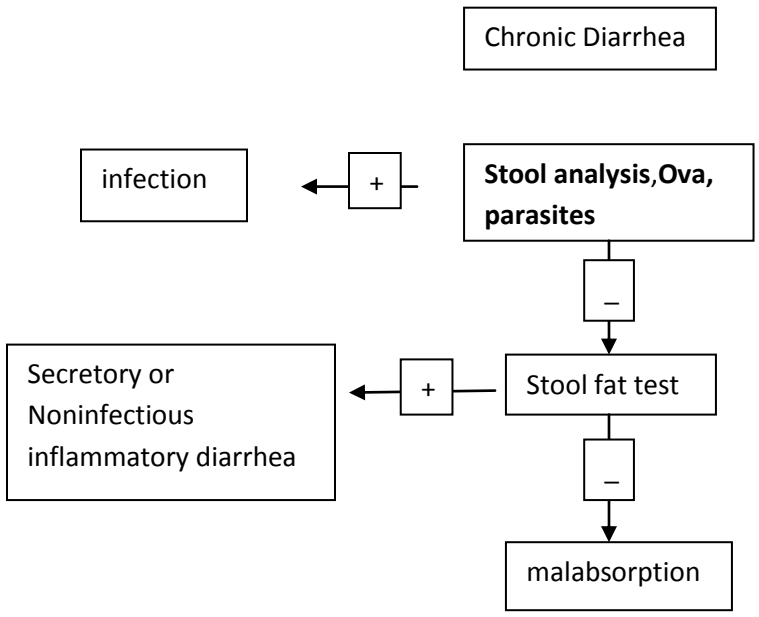
Chronic diarrhea

1. **Infection** ---------- **e.g.***Giardia lamblia* . AIDS often have chronic infections of their intestines that cause diarrhea.
2. **Post-infectious.** Following acute viral, bacterial or parasitic infections
3. **Malabsorption**
4. **Inflammatory bowel disease (IBD)**
5. **Endocrine diseases.**
6. **Colon cancer**
7. **Irritable bowel syndrome.**

Complications

1. Fluids ……Dehydration
2. Electrolytes …….. Electrolytes imbalance
3. *Sodium bicarbonate…….* Metabolic acidosis
4. If persistent ……Malnutrition





Malabsorption Syndrome

Inability of the intestine to absorb nutrients adequately into the bloodstream.

Impairment can be of single or multiple nutrients depending on the abnormality.

Physiology

The main purpose of the gastrointestinal tract is to digests and absorbs nutrients (fat, carbohydrate, and protein), micronutrients (vitamins and trace minerals), water, and electrolytes

Mechanisms and Causes of Malabsorption Syndrome

You DON'T have to memorize them

Inadequate digestion

- Postgastrectomy
- Deficiency of pancreatic lipase
- Chronic pancreatitis
- Cystic fibrosis
- Pancreatic resection
- Zollinger-Ellison syndrome

Deficient bile salt

- Obstructive jaundice
- Bacterial overgrowth
- Stasis in blind loops, diverticula
- Fistulas
- Hypomotility states (diabetes)
- Terminal ileal resection
- Crohns' disease
- Precipitation of bile salts (neomycin)

Primary mucosal abnormalities

- Celiac disease
- Tropical sprue
- Whipple's disease
- Amyloidosis
- Radiation enteritis
- Abetalipoproteinemia
- Giardiasis

Inadequate small intestine

- Intestinal resection
- Crohn's disease
- Mesenteric vascular disease with infarction
- Jejunoileal bypass

Lymphatic obstruction

- Intestinal lymphangiectasia
- Malignant lymphoma
- Macroglobulinemia

Pathophysiology

Inadequate digestion (**mainly**) or Small intestine abnormalities =Malabsorption

1- Inadequate digestion

Stomach Postgastrectomy

Pancreas Deficiency of pancreatic lipase-Chronic pancreatitis-Cystic fibrosis-Pancreatic resection

Bile Obstructive jaundice -Terminal ileal resection

2- Small intestine abnormalities

Mucosa Celiac disease-Tropical sprue -Whipple's disease-Giardiasis

Inadequate small intestine Intestinal resection-Crohn's disease

Lymphatic obstruction Intestinal lymphangiectasia- Malignant lymphoma

Cystic fibrosis = the secretion became think especially in lungs because abnormal transport of Cl and Na (genetic disease

Tropical sprue= malabsorption disease commonly found in the tropical regions, marked with abnormal flattening of the villi

Giardiasis = is parasite covered mucosa prevent absorption especially in duodenum.

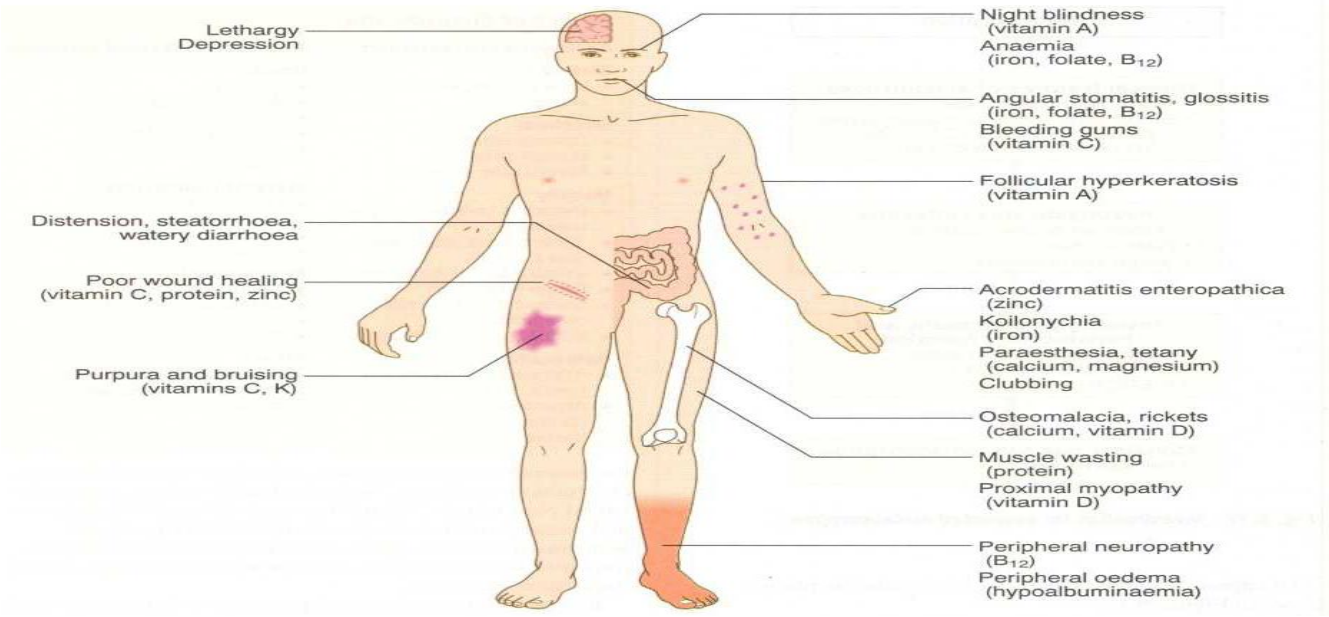
Crohn's disease = inflammatory bowel disease that may affect any part of the gastrointestinal tract from mouth to anus

Intestinal lymphangiectasia = dilatation of lymph vessels .

Clinical features

- Abnormal stools (large amount of fat)
- Failure to thrive or poor growth in most but not all cases
- Specific nutrient deficiencies, either singly or in combination.
- There is increased fecal excretion of fat (steatorrhea)
- Steatorrhea is passage of soft, yellowish, greasy stools containing an increased amount of fat.
- Growth retardation, failure to thrive in children
- Weight loss despite increased oral intake of nutrients.

Clinical features



Clinical futures Depend on the deficient nutrient

Protein	Swelling or edema Muscle wasting
B12, folic acid and iron deficiency	Anemia - fatigue and weakness
vitamin D, calcium	Muscle cramp -Osteomalacia and osteoporosis
vitamin K and other coagulation factor	Bleeding tendencies

Diagnosis

There is no specific test for malabsorption.
Investigation is guided by symptoms and signs.

1. Fecal fat study to diagnose steatorrhoea
2. Blood tests
3. Stool studies
4. Endoscopy (Biopsy of small bowel) why? To exclude celiac disease.

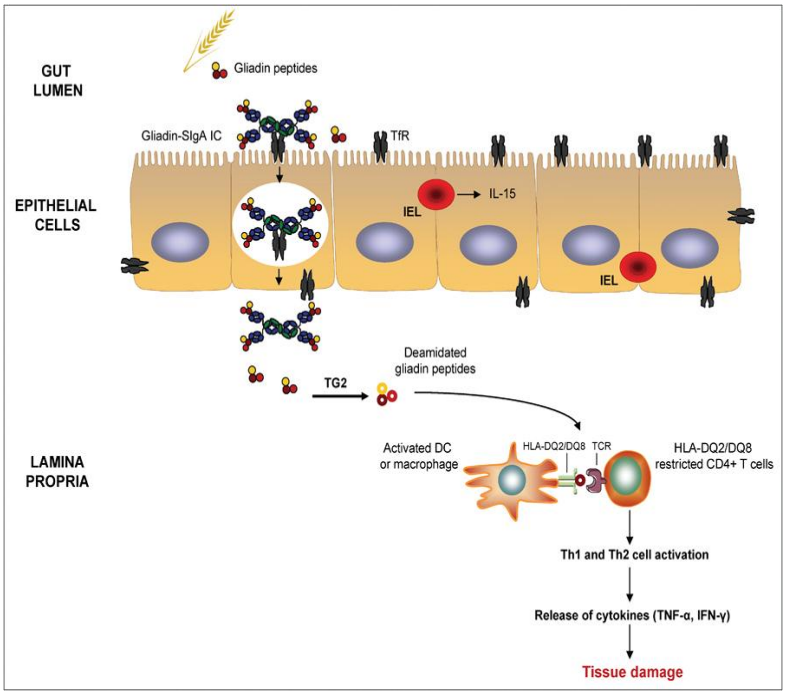
Malabsorption Syndrome

Celiac disease (**Gluten sensitivity – celiac sprue)**

An immune reaction to gliadin fraction of the wheat protein gluten
Usually diagnosed in childhood – mid adult.

Patients have raised antibodies to gluten autoantibodies
Highly specific association with class II HLA DQ2 (haplotypes DR-17 or DR5/7) and, to a lesser extent, DQ8 (haplotype DR-4).

a 33-amino acid gliadin peptide that is resistant to degradation by gastric, pancreatic, and small intestinal proteases
Gliadin is deamidated by tissue transglutaminase
deamidated gliadin peptides induce epithelial cells to produce the cytokine IL-15, which in turn triggers activation and proliferation of CD8+ intraepithelial lymphocytes that can express the MIC-A receptor NKG2D.



Clinical features Celiac disease

Typical presentation

GI symptoms that characteristically appear at age 9-24 months(fully development of the disease).

Symptoms begin at various times after the introduction of foods that contain gluten.

A relationship between the age of onset and the type of presentation;

Infants and toddlers-- GI symptoms and failure to thrive

Childhood-- minor GI symptoms, inadequate rate of weight gain,

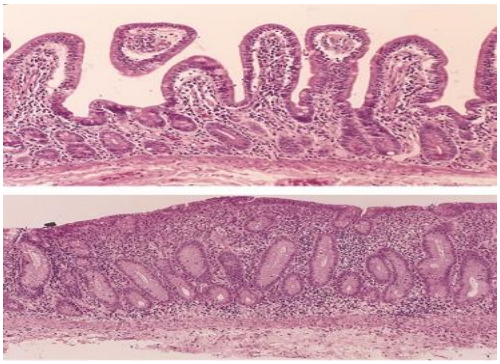
Young adults-- anemia is the most common form of presentation.

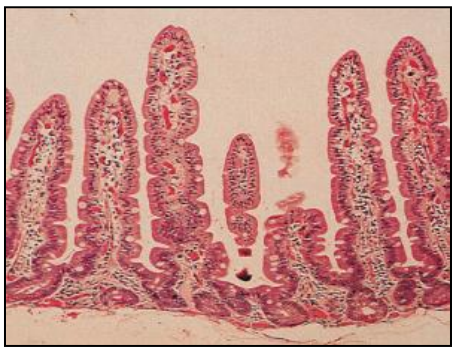
Adults and elderly-- GI symptoms are more prevalent

Histology

Mucosa is flattened with marked villous atrophy. (atrophy of villi)

Increased intraepithelial lymphocytosis





Diagnosis

Clinical documentations of malabsorption.

Stool --increase fat

Small intestine biopsy demonstrate villous atrophy.

Improvement of symptom and mucosal histology on gluten withdrawal from diet.(wheat, barley, flour

Other grains, such as rice and corn flour, do not have such an effect.)

Complications

Osteopenia , osteoporosis

Infertility in women

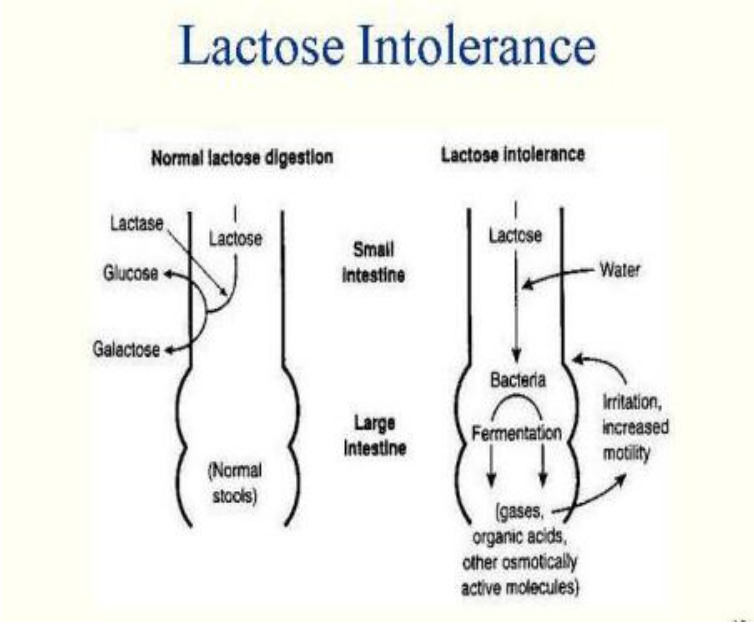
Short stature, delayed puberty, anemia,

Malignancies,[intestinal T-cell lymphoma] 3% develop T-cell lymphoma as a complication.

10 to 15% risk of developing GI lymphoma.

Celiac sprue : extra information

Autoimmune –mediated intolerance of gliadin (wheat) leading to steatorrhea. Associated with people of northern European descent. finding include antibodies to gliadin and tissue transglutaminase , blunting of villi and lymphocytes in lamina propria decrease mucosal absorption that primarily after jejunum .serum levels of tissue transglutaminase antibodies are used for screening .associated with dermatitis herpetiformis ,moderately increase risk of malignancy (e.g T cell lymphoma).



Lactose Intolerance

Low or absent activity of the enzyme lactase

Pathophysiology

At the brush border of enterocytes (lactase) convert lactose into glucose + galactose

Causes

1) Inherited lactase deficiency (rare)

a)Congenital lactase deficiency

Extremely rare

b)Childhood-onset and adult-onset lactase deficiency

Common -Genetically programmed progressive loss of the activity of the small intestinal enzyme lactase.

2) Acquired lactase deficiency

Transient - Secondary lactase deficiency due to intestinal mucosal injury by an infectious, allergic, or inflammatory process

Clinical

Bloating, abdominal discomfort, and flatulence

1 hour to a few hours after ingestion of milk products

Diagnosis

Empirical treatment with a lactose-free diet, which results in resolution of symptoms;
Hydrogen breath test

Hydrogen breath test .

- An oral dose of lactose is administered
- The sole source of H_2 is bacterial fermentation;
- Unabsorbed lactose makes its way to colonic bacteria, resulting in excess breath H_2.
- Increased exhaled H_2 after lactose ingestion suggests lactose malabsorption.

A 3-week trial of a diet that is free of milk and milk products is a satisfactory trial to diagnose lactose intolerance

Lactose intolerance

Summary

- Deficiency/absence of the enzyme lactase in the brush border of the intestinal mucosa → maldigestion and malabsorption of lactose
- Unabsorbed lactose draws water in the intestinal lumen
- In the colon, lactose is metabolized by bacteria to organic acid, CO2 and H2; acid is an irritant and exerts an osmotic effect
- Causes diarrhea, gaseousness, bloating and abdominal cramps

Defective Intraluminal Digestion
Digestion of fats and proteins
Pancreatic insufficiency, due to pancreatitis or cystic fibrosis
Zollinger-Ellison syndrome, with inactivation of pancreatic enzymes by excess gastric acid secretion
Solubilization of fat, due to defective bile secretion
Ileal dysfunction or resection, with decreased bile salt uptake
Cessation of bile flow from obstruction, hepatic dysfunction
Nutrient preabsorption or modification by bacterial overgrowth
Distal ileal resection of bypass
Total or subtotal gastrectomy
Primary Mucosal Cell Abnormalities
Defective terminal digestion
Disaccharidase deficiency (lactose intolerance)
Bacterial overgrowth, with brush-border damage
Defective transepithelial transport
Abetalipoproteinemia
Reduced Small Intestinal Surface Area
Gluten-sensitive enteropathy (celiac disease)
Short-gut syndrome, after surgical resections
Crohn disease
Infections
Acute infectious enteritis
Parasitic infestation
Tropical sprue
Whipple disease
Lymphatic Obstruction
Lymphoma
Tuberculosis and tuberculous lymphadenitis

This schedule from robbins page 610

Questions

which one of the following clinicopathologic findings is most consistently seen in malabsorption syndromes ?

A. hypercalcemia
B. hyperuricemia
C. iron overload
D. steatorrhea

A 16 years old secondary school female student was referred by her school doctor because of diarrhea and iron deficiency anemia . Following several investigation, she was diagnosed as a cause of malabsorption syndrome. which one of the following will be the most likely the finding , if a biopsy is taken from her intestine ?

A. atrophy of large bowel mucosa
B. intestinal lymphoid follicular hyperplasia
C. multiple duodenal ulcers
D. small intestine villous atrophy

A 34 year old man presents with weight loss, steatorrhea and flatulence. jejunal biopsy demonstrates flat intestinal villi with intraepithelial lymphocytes. This patient condition may improve with removal of which of the following items from his diet ?

A. beef
B. egg
C. wheat
D. tomatoes

A 10-month-old, previously healthy male infant develops a severe, watery diarrhea 2 days after visiting the pediatrician for a routine checkup. The most likely diagnosis is

A. Rotavirus infection
B. Enterotoxigenic *E. coli infection*
C. *Entamoeba histolytica infection*
D. Lactase deficiency
E. Ulcerative colitis

A 44 year old man is admitted to a hospital with an acute upper GI bleeding due to several gastric and duodenal ulcers seen in endoscopy. One of the duodenal ulcers is in the third portion of the duodenum. The patient also complains of a 1 year history of frequent non bloody diarrhea. A fecal osmotic gap is very low.

What type of diarrhea he has?

A. Osmotic
B. Secretory
C. Oxidative
D. Motility related

D,D,C,A,B